

Additional DHB Services

Used to Treat Symptoms of Adverse Reactions

GSK Eltroxin New Formulation



New Zealand Thyroid Association

THE REAL COST OF ELTROXIN

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The Real Cost of GSK Eltroxin

Introduction

Since the introduction of the new formulation of Glaxo Smith Kline (GSK) Eltroxin, many users have reported adverse reactions. These adverse reactions vary in severity. Many users, of the public health service, have found themselves placing a greater than normal burden on this system. For most, this demand has only occurred since the introduction of the new GSK Eltroxin.

This document outlines the results of a survey of 24 users of the new formulation of GSK Eltroxin. GSK Eltroxin has slowly filtered into the New Zealand thyroid users group as stocks of the old formulation were replaced. This survey covers the period from April 2008 to present day. Respondents were asked the treatment/s and clinics they had received / visited for (what they now know to be) adverse reactions to GSK Eltroxin.

These known adverse reactions have been relieved with the discontinuation of thyroid replacement therapy (TRT) that includes GSK Eltroxin. No one reported these symptoms prior to the commencement of GSK Eltroxin.

Participants were selected at random from a gathering of 180 thyroid replacement therapy users held 04/10/08. All the respondents have experienced adverse reactions to the new formulation of GSK Eltroxin. Many have sourced alternatives to this Pharmac subsidised TRT.

Some have found themselves unable to work - due to their adverse reactions to GSK Eltroxin. These people are unable to fund unsubsidised TRT. The same is true of those retired folk on fixed incomes.

No particular criteria were used when selecting survey respondents. Legible handwriting was the factor in the selection process. Accuracy and details of services used were another consideration. Responses, such as "Saw leg specialist", were not included in these results. Also not included were common ailments like colds or flu.

There is no distinct age group. Respondents range in age from 18 years old to over 70.

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Table of Results

Service Used	Frequency (for the year before New Formulation)	Since New Eltroxin Formulation (04/08 as a universal start date)		
Laboratory Tests	18	77		
Physiotherapy	10	89		
Neurology	1	8		
M.R.I.	0	3		
C.A.T. Scans	0	2		
X -Ray	2	18		
A & E Visits	1	12		
Hospital Admissions	2	4		
Rheumatology	1	10		
Immunology / Allergy	0	15		
ENT	1	6		
Cardiology	1	6		
Mental Health and Counselling	2	47		
Gynaecology	3	13		
Dermatology	0	7		
Endocrinology	1	3		
Ophthalmology	1	4		
Gastroenterology	1	4		
Pharmaceuticals	7	132		
Totals of Services	Pre Eltroxin	52	Post Eltroxin	460

Adverse Reactions Warning

The MedSafe data sheet explains “the following effects are indicative of excessive dosage and usually disappear on reduction of dosage or withdrawal of treatment for a few days. Anginal pain, cardiac arrhythmias, palpitation, and cramps in skeletal muscle; tachycardia, diarrhoea, vomiting, tremors, restlessness, excitability, insomnia, headache, flushing, sweating, excessive loss of weight and muscular weakness. Rarely hypersensitivity reactions such as skin rash and pruritus have been reported. “

These are common symptoms if an excessive dose has been administered. Our experiences show these reactions are not dependent on dosage. Nor are they the only symptoms experienced by our participants.

Many of our respondents exhibited signs of hypothyroidism: low energy, constant tiredness, depression, dizziness, weight gain, intolerance to cold, inability to concentrate, memory lapses, constipation, raised blood cholesterol, muscle weakness, cramps, menstrual irregularities, dry scaly skin and brittle nails, decreased sex drive, impaired coordination.

The large majority experienced both hyper and hypo thyroid symptoms. These symptoms, and many others, have been reported to CARM by over 1,100 New Zealanders.

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Laboratory Tests

It is interesting to note that only 3 respondents were referred to Endocrinology. Many questioned their G.P.s as to the possibility of the symptoms they were displaying that also coincided with the commencement of the new formulation of GSK Eltroxin. Blood tests, conducted by the G.P.s, returned results within normal range. Any connection, to a side effect of GSK Eltroxin, remained undiagnosed. Further laboratory investigations were conducted for each exhibited symptom.

Physiotherapy

Sore joints, neck pain and stiffness, general muscle weakness / aches and pains, dizziness, vertigo, inability to lift the arms, have all been treated at physiotherapy departments. Many have reported whole body aches and pains. This figure does not include massage from private sector practitioners, chiropractic, osteopathic or acupuncture treatments. Including those treatments would more than quadruple the alarming figure of 89. All these symptoms have been eliminated, or greatly reduced, with the discontinuation of GSK Eltroxin.

Neurology

Brain fog, headaches, light headedness, confusion, intolerance to light, cold, heat, migraine symptoms have resulted in trips to Neurology. 3 survey participants underwent M.R.I. and 2 had C.A.T. scans. The symptoms, requiring such investigation, have generally been resolved amongst those ceasing GSK Eltroxin.

X-Ray

Joint pain, swelling, and arthritic symptoms have required X-Ray. Suspected carpal tunnel syndrome has also required the services of the X-Ray department. Although no one was actually diagnosed with carpal tunnel syndrome, their symptoms warranted such investigation. One of our respondents reports having 6 different parts of his anatomy X-Ray'd within a 5 month period (2 of these during an acute visit to A&E). No cause of his pain was identified. The symptoms have been resolved since accessing an alternative TRT to GSK Eltroxin.

Accident and Emergency – Hospital Admissions

A&E visits for swollen, painful joints, chest pain, irregular heart beat, and crippling pain have all been reported in this survey. Several of the symptoms, pertaining to the cardio system, resulted in admission to hospital. Further investigation revealed no abnormalities.

When accompanied by mental confusion and brain fog, it is easy to convince someone they may not remember injuring themselves. A swollen painful joint is alarming to family members – particularly when their loved one cannot recall the injury. It is probable no accident actually occurred to explain the perceived injury. Outside of G.P.'s business hours, these conditions have resulted in visits to A&E departments. Medical emergencies have subsided with the discontinuation of GSK Eltroxin.

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Rheumatology

Nothing definitive has been diagnosed amongst those referred to Rheumatology. While joint pain and stiffness, swelling and loss of movement present as symptoms, all usual diagnostic techniques have failed to determine the cause. X-Ray, blood screening for rheumatoid agents and, referrals to physiotherapy have been unsuccessful to identify the cause of these problems. Limited results have been reported with regards the effectiveness of the treatments.

It has also been concluded that some clients have the condition fibro myalgia.

Most of these symptoms have dissipated or been completely eliminated with the removal of GSK Eltroxin.

Immunology - Allergies

People, who have never suffered environmental allergies, reported the need for nasal sprays and other treatments such as - antibiotics and antihistamines, to treat symptoms. They did not respond as their G.P.'s hoped, they were referred to immunology. Others developed further complications and required additional treatment and, in one case, surgery. Normal sinus function returned, and the need for environmental allergy treatments dissipated, upon the cessation of GSK Eltroxin.

Cardiology

Varying degrees of cardiac investigations were required by some of those surveyed. Presentation at A&E, with chest pain, resulted in 2 hospital admissions. Nothing was found to be wrong with these respondents. Other's were referred to cardiology by their G.P.'s due to palpitations, high blood pressure or suspected cardiac problems.

A common theme amongst most recipients is elevated blood pressure and higher than normal, cholesterol. None have had these elevations prior to the commencement of GSK Eltroxin. Those who have discontinued GSK Eltroxin have found an almost immediate reduction in these higher than normal readings.

Mental Health Services and Counselling

Mental Health Services have been utilised by those unable to deal with their adverse reaction to GSK Eltroxin – particularly when they did not know an adverse reaction (of this magnitude) was possible.. Depression and suicidal feelings have been noted as a side effect of GSK Eltroxin. The respondents' demeanour was so outside the "normal self", family members have feared for the mental state of the loved one (taking GSK Eltroxin) and have called the crisis team. Suicidal feelings have been reported by many of those people taking GSK Eltroxin though only 4 are included in this survey. There was no evidence of this condition before the introduction of GSK Eltroxin.

Many of our respondents have been and still are on anti depressants. These people have only found it necessary to begin a regimen of antidepressants since their thyroid replacement therapy has been replaced by GSK Eltroxin. Only 2 of these people have reported they have ceased antidepressants since finding an alternative to GSK Eltroxin.

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Gynaecology

Menstrual disturbances are NOT noted on the list of adverse reactions from GSK – although many women have found this to be the case. Women, one as young as 18, have reported disturbances (and complete cessation) to their menstrual cycles when using GSK Eltroxin.

Bioequivalency testing, conducted by MedSafe, was over a 48 hour period (no pun intended). A menstrual cycle, of 48 hours, would be of concern in itself.

Not all women experiencing menstrual disturbances are of menopausal age. Nor do their blood tests show the onset of menopause. Yet menstrual disturbance has been reported by pre-menopausal women. Normal cycles have been restored with the discontinuation of GSK Eltroxin.

Dermatology

Many reported strange rashes and skin conditions such as peeling hand, dry skin and various other skin distortions while on GSK Eltroxin. One respondent had a condition so severe, skin infections developed. Many of these conditions were relieved or eliminated by those fortunate to have access to an alternative TRT to GSK Eltroxin.

Endocrinology

As covered in paragraph 2. The side effects and adverse reactions, as listed by GSK in their handout to G.P.'s, were somehow overlooked when dealing with thyroidian's presenting with those symptoms and conditions. Hence, very few were referred to Endocrinology. Those new to thyroid replacement therapy were more likely to have visited Endocrinology than those long term TRT users exhibiting adverse reactions to GSK Eltroxin.

Ophthalmology

Visual disturbances are not usually associated with thyroid problems. However, an overwhelming number of those surveyed reported major eye problems while on GSK Eltroxin. These included dry, sore, itchy eyes and visual disturbances. Many required examination, either privately or within the public health system. Others failed eye tests and found themselves bespectacled (an expense proven unnecessary). Normal eyesight and function has been restored since GSK Eltroxin has been omitted from their pharmaceutical regimen.

Gastroenterology

GSK advise constipation, abdominal pain and, diarrhoea, are symptoms of adverse reactions to GSK Eltroxin. Some respondents have been referred, by their G.P.s, to Gastroenterology. While this is a highly respected department, it is seldom a person's first choice of a place to visit on a nice, sunny, day. "Oh! I think I'll have a colonoscopy, today!"

Many others reported gastric reflux currently being treated with Losec – a substance that is known to interfere with the absorption of TRT.

All reported gastro-intestinal problems have ceased with the discontinuation of GSK Eltroxin.

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Pharmaceuticals

This report only refers to additional medications required by respondents since the introduction of the new formulation of GSK Eltroxin. These pharmaceutical costs could well be called an *own goal!* Any savings Pharmac may have made, with the introduction of GSK Eltroxin, have certainly been absorbed by the related costs of the pharmaceutical products used in the treatment of the symptoms of adverse reactions. These include, antidepressants, pain relief, eye creams and drops, HRT's, antiinflammatories, and anything possible that could be prescribed by any of the aforementioned departments and G.P.'s to treat symptoms of adverse reactions. Most of these pharmaceutical costs are eliminated by the termination of GSK Eltroxin as a thyroid replacement therapy.

Bio Equivalency Testing

Bio equivalency testing, conducted by MedSafe, showed these results.

“The purpose of a bioequivalence trial is to compare the relative bioavailability of two products, but it is standard practice to monitor and report adverse events that occur during bioequivalence studies.

All adverse events were of mild to moderate intensity. Adverse events considered treatment related by the investigator occurred more frequently after the administration of the reformulated product (10 adverse events in 8 of 36 subjects) than after the reference product (3 adverse events in 3 of 36 subjects) and are detailed in the table below:

Drug-Related Adverse Events

		Treatment:	
Adverse Event	Total*	Reference Product	Reformulated Product
Headache	6	2	5
Malaise & Fatigue	2	1	1
Sweating	2	0	2
Diarrhoea	1	0	1
Abdominal Discomfort & Pain	1	0	1
Number of adverse events	12	3	10
Number of subjects with adverse events	9	3	8
Number of subjects exposed	36	36	36

* Adverse events that were ongoing over both treatment periods were counted for each treatment period, but only once in the total column.

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No adverse event persisted beyond the end of the study. No serious adverse event or death was observed during the study and no subject was withdrawn from treatment due to an adverse event.”¹

Notice approximately 25% of participants showed signs of an adverse reaction to the new formulation of GSK Eltroxin. It seems strange that in a profession - based on Hippocrates guiding principle of “Do no harm”- GSK Eltroxin was released under such test results.

Of the 70,000 TRT users in New Zealand, this figure of 25% potentially means 17,500 could suffer adverse reactions in varying degrees.

Many of our respondents did not immediately experience adverse reactions to GSK Eltroxin. In some cases, side effects were not experienced till weeks after the change to the new formulation. This begs the question – how many adverse reactions would have been detected if the trial had been conducted over a longer period of time?

It is clear there have been adverse reactions to GSK Eltroxin not explained by the “mass hysteria” comments of those responsible for the introduction of the newly formulated TRT.

American Thyroid Association

“Adverse Drug Experience Reports, citing serious clinical consequences, brought to light problems with preparation potency (both under and over), stability, and consistency in lot-to-lot bioavailability. In some instances, reformulations with different excipients (including colour agents and fillers that were generally thought to be inert) proved to be responsible for some within brand variations.

By 1997, the FDA concluded that no marketed levothyroxine preparation had been shown to have consistent potency and stability and therefore could not be recognized by the FDA as “safe and effective.” In light of this, the FDA ruled that an NDA would be required in order to market a levothyroxine product after August 14, 2000, and those pre-existing products that were “non-NDA approved” could only be distributed until August 14, 2001.”²

FDA testing has already approved Gold Shied and Synthroid as acceptable bioequivalent TRT’s

Employment

4 people reported job loss or inability to work since the introduction of GSK Eltroxin.

¹ http://www.parliament.nz/NR/rdonlyres/339D6827-B56D-4A75-B251-9C8FAA2C3BC8/93497/QWA_0771820087718attachment1.pdf - viewed online - 06/10/08

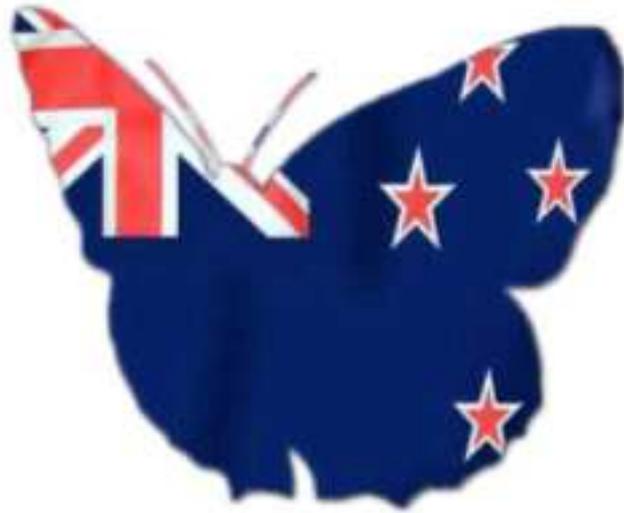
² http://www.thyroid.org/professionals/advocacy/04_12_08_thyroxine.html - viewed online - 06/10/08

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Conclusion

It is clear with the introduction of GSK Eltroxin an extra burden has been placed on all aspects of the public health system. Those now unable to work are neither productive nor contributing with their usual tax dollars to funding our public health system.

We request your support in the immediate removal of the new formulation of GSK Eltroxin and the implementation of 2 subsidised synthetic thyroid replacement therapies – Gold Shield and Synthroid – and the natural replacement therapy – Whole Thyroid Extract (W.T.E.).



New Zealand Thyroid Association